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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/486,334	07/18/00	DROUX M	PH-98/080

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EXAMINER	
KUBELIK,A	
ART UNIT	**PAPER NUMBER**
1638	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/486,334	Applicant(s) DROUX ET AL.	
	Examiner Anne Kubelik	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above claim(s) *7,10,11,14-16,21,22 and 31-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9,12,13,17-20 and 23-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 July 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group III (claims 1-30, drawn to SEQ ID NO:1 or SAT 3) in Paper No. 9 is acknowledged.

Applicant mistakenly believes that the election requirement for a sequence was a species election requirement. That is incorrect. The restriction requirement mailed 05 June, 2001, indicates that that it was a restriction requirement (pg 1, line 11).

The traversal is on the ground(s) that the different serine acetyltransferase (SATase) sequences are used in the same way.

This is not found persuasive because nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute **independent and distinct** inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq (see MPEP 803.04 and 2434). Thus, methods of using each of these sequences constitute independent and patentably distinct inventions.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7, 10-11, 14-16 and 21-22 are drawn to sequences other than the elected sequence, SEQ ID NO:1, which encodes the cytoplasmic SATase, SAT3. Thus, they and 31-59 are withdrawn from consideration, as being drawn to nonelected inventions. Claims 1-6, 8-9, 12-13, 17-20 and 23-30 are examined.

Drawings

2. The drawings are objected to for the reasons indicated on accompanying form PTO 948. Note also that the legends in the figures should be in English. Correction is required.

Specification

3. A substitute specification including the claims is required pursuant to 37 CFR 1.125(a) for the following reasons:

Dark smudges on the pages could result in printing errors.

The SEQ ID NOs: in the specification do not correspond to the current SEQ ID NOs: in the sequence listing. Additionally, the oligonucleotides should also be identified by SEQ ID NO:, as required by 37 CFR 1.821(d). In the Office action, all references to SEQ ID NO:1 are to SEQ ID NO: as currently listed in the sequence listing and computer readable form, not to SEQ ID NO: as listed in the specification.

A substitute specification filed under 37 CFR 1.125(a) must only contain subject matter from the original specification and any previously entered amendment under 37 CFR 1.121. If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and must be accompanied by: 1) a statement that the substitute specification contains no new matter; and 2) a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

4. The disclosure is objected to because it contains embedded hyperlinks and/or other forms of browser-executable code. Applicant is required to delete the embedded hyperlinks and/or other forms of browser-executable code. See MPEP § 608.01.

5. The abstract of the disclosure is objected to because of use of legal phraseology such as "said." Additionally, the title of the invention should not be located on the abstract page and the abbreviation "SAT" should be defined. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6, 8, 12-13, 17-20 and 23-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain methods of increasing the production of cysteine, glutathione, methionine and sulfur derivatives in a plant by overexpressing a plant SATase, does not reasonably provide enablement for methods of increasing the production of cysteine, glutathione, methionine and sulfur derivatives in a plant by overexpressing a cysteine-sensitive SATase, by overexpressing an SATase by mitochondrial transformation, for mutagenesis of a plant SATase, for expressing in the cytoplasm of an SATase encoded by the chloroplast, or for chloroplast targeting via use of an optimized transit peptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to methods of increasing the production of cysteine, glutathione, methionine and sulfur derivatives in a plant by overexpression of a plant SATase

that include overexpressing one from any plant, one made cysteine insensitive by mutagenesis, by transformation of a SATase gene into a plant mitochondrion, by expression in the cytoplasm of an SATase encoded by the chloroplast, and by targeting of SATase to the chloroplast via use of an optimized transit peptide.

The claims are drawn to a method of overexpressing an SATase by transformation into a plant an SATase, either cysteine-sensitive or cysteine insensitive, from any plant. The instant specification, however, fails to provide guidance for genes encoding SATases from any source. It also fails to provide guidance for methods of increasing the production of cysteine, glutathione, methionine and any sulfur derivative by overexpression of a cysteine-sensitive SATase. The instant specification even states that cysteine induced inhibition of SATase is a limiting factor in the synthesis of cysteine (pg 8, lines 4-10). As no working examples are provided of overexpression of a cysteine sensitive SATase resulting in increased production of cysteine, unpredictability is not overcome.

Claim 12 is drawn to a method of overexpressing an SATase in the mitochondria. This would include overexpression by transformation of the mitochondria with a gene encoding an SATase. However, the instant specification fails to teach mitochondrial transformation, and mitochondrial transformation in plants is unpredictable. A general lack of characterization of the plant mitochondrial genome (see, *e.g.*, Palmer, et al, 1994, pg 37-62, in Meyerwitz et al, ed., *Arabidopsis*, Cold Spring Harbor Press, see pg 44-52) prohibits homologous recombination constructs and a lack of understanding of mitochondrial gene expression means that expression of any inserted DNA is unpredictable.

Claim 5 is drawn to a method of overexpressing a mutated plant SATase. The instant specification, however, fails to provide guidance for which amino acids of the SATase can be altered and to which other amino acids, and which amino acids must not be changed, to maintain SATase activity and convert a cysteine-sensitive SATase to a cysteine-insensitive one. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results in protein mutagenesis. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). The instant specification also fails to provide working examples of mutagenesis of a plant SATase; thus, unpredictability is not overcome.

Claim 18 is drawn to a method of overexpressing an SATase by transformation of a gene encoding an SATase into the chloroplast. However, claim 6, a claim upon which claim 18 depends (via claim 17) is drawn to overexpressing that SATase in the cytoplasm. The instant specification fails to provide guidance for methods of transformation of the chloroplast that

would direct the encoded protein out of the chloroplast and into the cytoplasm. Currently, it is only possible to transform the nucleus with a gene encoding a gene linked to a transit peptide that results in the gene product being translated in the cytoplasm and transported into the chloroplast; the opposite is not currently possible.

Additionally, Turk et al (1997, New Phytol. 136:29-38) teach that a targeting sequence sufficient for translocating one protein to a cellular organelle was unable to direct another to that same organelle (pg 36, left column). Thus, targeting sequence themselves are also unpredictable.

Claims 27-30 are drawn to a method of overexpressing an SATase presumably by transformation of a plant with a DNA construct comprising an SATase gene fused to a DNA sequence encoding a chloroplast transit peptide plus additional amino acids, thereby making an optimized transit peptide (OTP). However, the instant specification fails to provide guidance for the sequence of any such OTP. It also fails to provide a plasmid that comprises the OTP used in the examples (for example, the one in Figure 11).

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate methods for increasing the production of cysteine, glutathione, methionine and sulfur derivatives in a plant by overexpression of a plant SATase that include overexpressing one from any plant, one made cysteine insensitive by mutagenesis, by transformation of a SATase gene into plant mitochondria, by expression in the cytoplasm of an SATase encoded by the chloroplast, and by targeting SATase to the chloroplast via use of an optimized transit peptide.

8. Claims 1, 6, 17,19, 23, 25 and 27-30 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ novel plasmids contained in microorganisms. These plasmids encode optimize transit peptides. Since the plasmid contained in the microorganism is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the plasmid contained in the microorganism is not so obtainable or available, the requirements of 35 USC 112 may be satisfied by a deposit of the microorganism. The specification does not disclose a repeatable process to obtain the plasmid contained in the microorganism and it is not apparent if the plasmid is readily available to the public. Thus, a deposit is required for enablement purposes.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the enforceable life of the patent, whichever is longer;
(d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and,
(e) the deposit will be replaced if it should ever become inviable.

9. Claims 1-6, 8, 12-13, 17-20 and 23-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to methods of overexpressing cysteine-insensitive and cysteine sensitive SATases wherein the SATase is from any organism, or is a mutant SATase, or is linked to an OTP. In contrast, the specification only describes a coding sequence from *Arabidopsis* that comprises SEQ ID NO:1. No description is provided for any SATases from any other organism, for any mutant SATases, nor any OTP.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, and given the high level of unpredictability in this art, one skilled in the art would not have been in possession of the genus claimed at the time this application was filed.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-6, 8-9, 12-13, 17-20 and 23-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

Dependent claims are included in all rejections.

It is unclear in these methods if overexpression occurs as a result of transformation with a nucleic acid encoding an SATase or if it occurs by some other mechanism. For purposes of examination all possibilities were assumed.

Claims 1-6, 8-9, 12-13, 17-20, 23-24, 27 and 29 are indefinite in their recitation of the abbreviation "SAT." For purposes of examination, it was assumed that "SAT" referred to "serine acetyltransferase." Such treatment does not relieve Applicant of the responsibility to respond to this rejection.

Claim 26 is indefinite in its recitation of the abbreviation "EPSPS." For purposes of examination, it was assumed that "EPSPS" referred to "5-enolpyruvylshikimate-3-phosphate synthase." Such treatment does not relieve Applicant of the responsibility to respond to this rejection.

Claim 1 is indefinite in its recitation of "consisting in overexpressing". "in" should be replaced with--of--.

Claims 1 and 18 are overly wordy in their recitation of "the said method" and "the said plant cells". It is not necessary to use both 'the" **and** "said", and it is much clearer to use only one of them.

Claim 1 is indefinite in its recitation of "sulphur derivatives thereof". It is unclear what these sulfur derivatives are, particularly because the manufacture of all sulfur compounds in a plant are interconnected.

Claim 3 is indefinite in its recitation of "native SAT of bacterial origin" as an SATase of bacterial origin would not be native to a plant.

Claim 5 is indefinite in its recitation of "rendered cysteine-insensitive by mutagenesis" as it is not clear if the phrase modifies "plant SAT", SAT of bacterial origin" or "mutated plant SAT". For purposes of examination, all were assumed.

Claims 3, 5 and 24 are indefinite in their recitation of "SAT of bacterial origin", and claim 24 is indefinite in its recitation of "SAT of plant origin". It is unclear if these SATases are wild-type or mutated genes; the use of the word origin suggests the SATase has been changed in some way. It would be better to replace the first with --bacterial SAT-- and the latter with--plant SAT--.

Regarding claims 8, 15 and 21, the phrase "in particular" renders the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed inventions. See MPEP § 2173.05(d).

In claim 9, it is unclear if the amino acid sequence or the nucleic acid sequence of SEQ ID NO:1 as originally filed is intended.

It is unclear how in the method of claim 10 that an SATase can be both overexpressed in the cytoplasm, as required by parent claim 6, and be a non-cytoplasmic SATase, as required by claim 10. Any SATase expressed in the cytoplasm would be a cytoplasmic SATase. It the SATase a mitochondrial SATase or a plastid SATase, then that should be stated.

Claims 12-13 are indefinite in their statement of the location of the expression of the SATase. Claim 12 states that the SATase is overexpressed in mitochondria, but claim 13, which is dependent upon claim 12, states that the SATase is overexpressed in the cytoplasm. Rewriting all the claims to detail the overexpression steps in more detail - transforming an SATase gene into the plant cell, regenerating the cell into a plant, expressing the gene in the plant, etc, with dependent claims describing the SATase gene in more detail - would eliminate some of the claim indefiniteness.

Similarly, claims 6 and 17 are also indefinite in their statement of the location of the expression of the SAT. Claim 6 states that the SATase is overexpressed in cytoplasm, but claim 17, which is dependent upon claim 6, states that the SATase is overexpressed in the chloroplast.

Claim 20 is indefinite in its recitation of "SAT is homologous with the transit peptide". This statement appears to mean that SATase is a transit peptide. Similarly claim 23 is indefinite in its recitation of "SAT is heterologous with the transit peptide". This statement appears to mean that SATase is a transit peptide from another plant species. Neither make any sense, and these claims could not be readily interpreted. For purposes of examination the claims were assumed to be identical to claim 19, the claim upon which they depend.

Claims 24 is indefinite in its recitation of "that the SAT is a cytoplasmic SAT of plant origin or an SAT of bacterial origin, and that the SAT is a plant SAT or a native SAT of bacterial origin." It is unclear how an SATase can be both a bacterial and a plant SATase, as would be the case if the SATase were both a cytoplasmic SATase of plant origin and a native SATase of bacterial origin, as is possible in the definition of this SATase.

Regarding claim 28, the phrases "preferably" and "more preferably" render the claim indefinite because it is unclear whether the limitation(s) following the phrases are part of the claimed invention. See MPEP § 2173.05(d).

Claims 27-29 are indefinite in their recitation of C-terminal and N-terminal portions of peptides and SATases, and claim 29 is indefinite in its recitation of "between the C-terminal portion of the N-terminal portion of the mature protein and the N-terminal portion of the SAT". It is not clear how much of the proteins comprise the C-terminal and N-terminal portions. Additionally, in claim 29 it is not clear where in the N-terminal portion the second transit peptide is located.

In claim 30 it is unclear to which transit peptide, the one described in claim 27 or the second one described in claim 29, is being referred in line 2.

12. Claims 1-6, 8-9, 12-13, 17-20 and 23-30 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Method steps must be circular; the final step must generate the item the method is intended to produce. For example, the method of increasing the production of cysteine, glutathione and methionine and sulfur derivatives thereof by plant cells and plants in claim 1 ends in overexpression of a SAT in plant cells and plants, when it should end in the production cysteine, glutathione and methionine and sulfur derivatives thereof by plant cells and plants.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1, 4-6, 8, 12-13 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Takahashi et al (1997, Proc. Natl. Acad. Sci. USA 94:11102-11107).

Takahashi et al teach that SAT1 is overexpressed in *Arabidopsis* upon sulfate starvation (pg 11105, right column, paragraph 2). SAT1 encodes an insensitive mitochondrial form of SATase and thus is expressed in the cytoplasm before transport to the mitochondria; after transport it would be expressed there.

15. Claims 1-3, 6, 8 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Saito et al (1997, Gene 189:57-63) in light of Noji et al (1998, J. Biol. Chem. 273:32739-32745).

Saito et al, 1997, teach that SATase is overexpressed in watermelon upon sulfur starvation and by addition of pyrazole (pg 60, paragraph spanning the columns and right column, paragraph 4). Noji et al teach that this SATase is a cytosolic form of SATase and is sensitive to cysteine (pg 32743, left column, paragraph 3, and pg 32744, left column, paragraph 3).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 1-6, 8, 12-13, 17, 19-20 and 23-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al (1994, Plant Physiol. 106:887-895) in view of Noji et al (*supra*).

The claims are drawn to a method of increasing the production of cysteine and other sulfur-containing compounds in a plant or plant cells by overexpressing an SATase in the cytoplasm, the mitochondria or the chloroplasts of the plant or plant cells.

Saito et al, 1994, disclose tobacco plants transformed with a construct encoding the spinach cytoplasmic cysteine synthase gene alone or fused to a Rubisco ssu transit peptide sequence (pg 889, right column, paragraph 3-5). The transit peptide-cysteine synthase constructs had an additional two amino acids between the transit peptide and the N-terminal portion of the cysteine synthase gene; these peptides would be the same as those from a mature N-terminal portion of a protein that is located in the plastids or would be the same as a second transit peptide. These constructs were properly transported to the chloroplast and correctly processed (pg 890, right column, paragraph 2). The resulting plants showed increased production of cysteine and resistance to sulfite (pg 891, left column, paragraph 2, to pg 892, left column paragraph 2). Saito et al do not disclose plants transformed with a construct encoding SATase.

Noji et al teach genes encoding cytoplasmic, chloroplastic and mitochondrial SATase genes from *Arabidopsis* and their overexpression of the genes in *E. coli* (pg 32742). The mitochondrial and chloroplastic forms would be fused to mitochondrial and chloroplastic transit peptides.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to increase the production of cysteine in a plant by overexpressing a cytoplasmic cysteine synthase in the cytoplasm and chloroplasts of a plant as taught by Saito et al, and to modify that to use another enzyme required for cysteine biosynthesis, SATase, as described in Noji et al. One of ordinary skill in the art would have been motivated to do so because of the role SATase has in regulation of cysteine biosynthesis Noji et al, pg 32744, left column, paragraph 4) and because substitution of one crucial enzyme for cysteine biosynthesis with another crucial enzyme for cysteine biosynthesis is an obvious design choice.

18. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al, 1994, in view of Noji et al as applied to claims 1-6, 8, 12-13, 17, 19-20 and 23-30 above, and further in view of Ruffet et al (1995, Eur. J. Biochem. 227:500-509).

The claim are drawn to a method of increasing the production of cysteine and other sulfur-containing compounds in a plant or plant cells by overexpressing an SATase of SEQ ID NO:2 in the cytoplasm, the mitochondria or the chloroplasts of the plant or plant cells.

Saito et al, 1994, in view of Noji et al disclose plants transformed with a construct encoding a cytosolic SATase gene fused to a Rubisco ssu transit peptide sequence. The resulting plants showed increased production of cysteine and resistance to sulfite. Saito et al, 1994, in view of Noji et al do not disclose plants transformed with a construct encoding a cytosolic SATase gene of SEQ ID NO:1 or encoding SEQ ID NO:2.

Ruffet et al teach an isolated nucleic acid encoding an SATase isoform from *Arabidopsis* that comprises SEQ ID NO:2.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to increasing the production of cysteine and other sulfur-containing compounds in a plant or plant cells by overexpressing an SATase by transformation with a gene encoding one SATase isoform as taught by Saito et al, 1994, in view of Noji et al, and to modify that to use another SATase isoform as described in Ruffet et al. One of ordinary skill in the art would have been motivated to do so because substitution of Arabidopsis SATase genes would be an obvious design choice and because the SATase taught by Ruffet et al is apparently cysteine-insensitive (pg 508, left column, paragraph 2).

19. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Saito et al, 1994, in view of Noji et al as applied to claims 1-6, 8, 12-13, 17, 19-20 and 23-30 above, and further in view of Svab et al (1993, Proc. Natl. Acad. Sci USA 90:913-917).

The claims are drawn to a method of increasing the production of cysteine and other sulfur-containing compounds in a plant or plant cells by overexpressing an SATase gene that is integrated into the chloroplasts of the plant or plant cells.

Saito et al, 1994, in view of Noji et al disclose plants transformed with a construct encoding a cytosolic SATase gene fused to a Rubisco ssu transit peptide sequence. The resulting plants showed increased production of cysteine and resistance to sulfite. Saito et al, 1994, in view of Noji et al do not disclose transformation of chloroplast with SATase gene-containing constructs.

Svab et al teach plastid transformation in tobacco (pg 914-915).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to increase the production of cysteine and other sulfur-containing compounds in a plant

or plant cells by transformation with a construct encoding a cytosolic SATase gene fused to a chloroplast transit peptide sequence as taught by Saito et al, 1994, in view of Noji et al, and to modify that transform the chloroplast as described in Svab et al. One of ordinary skill in the art would have been motivated to do so because the introduction of protein into the chloroplast by chloroplast transformation or by nuclear transformation with a construct that has a chloroplast transit peptide is an obvious design choice.

Conclusion

20. No claim is allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached on Monday through Friday, 8:15 am - 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula K. Hutzell, can be reached on (703) 308-4310. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne R. Kubelik, Ph.D.
September 6, 2001

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638

Attachment for PTO-948 (Rev. 03/01, or earlier)
6/18/01

The below text replaces the pre-printed text under the heading, "Information on How to Effect Drawing Changes," on the back of the PTO-948 (Rev. 03/01, or earlier) form.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

1. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

2. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a).

Failure to take corrective action within the set period will result in **ABANDONMENT** of the application.